allegedly not clear. Claims 1-3, 6-13, 15, 16, 20-26, 28, 29, 32, 34-40 and newly added claims 47, 50, 51 have been rejected under 35 U.S.C. §102(e) as allegedly anticipated by Patterson et al, U.S. 6,156,729 ("Patterson, et al."). Claims 1-3, 6-18, 20-26, 28-30, 32, 34-55 and newly added claims 44-55 were rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Patterson, et al. in view of Cleland (Crit. Rev. Therapeutic Drug Carrier Systems, 1993 Vol.10, pp307-377, hereinafter "Cleland").

This Response addresses each of the Examiner's rejections. Applicants therefore respectfully submit that the present application is in condition for allowance. Favorable consideration of all pending claims is therefore respectfully requested.

The amendment filed January 11, 2002 has been objected to under 35 U.S.C. §132 as allegedly introducing new matter.

In response, and in an effort to expedite favorable prosecution, applicants have amended the specification as follows:

Applicants have deleted "additives for maintaining pH and isotonicity" beginning at Page 2, Line 21 and ending at Page 2, Line 22. The paragraphs beginning at Page 5, Line 10 and ending at Page 5, Line 25 has been removed. The phrase "and/or additives" at Page 10, line 23 has been deleted as has "and other ingredients of the composition" at Page 11, line 33. Applicants have also deleted "preservatives" and replaced the same with "bactericides" on page 12. The word "additives" has been replaced with "stabilizing agents" on page 14. Applicants have reinserted "0.05 or" on page 49, and reinserted "The least was the pH5 citrate buffer containing only sorbitol and pH 5.5 citrate containing sorbitol and Tween 80 was somewhere in the middle", at the end of the paragraph describing Ion Exchange results at page 49. No new matter has been added.

Applicants believe that the words "At pH 5.0" at Page 24, Line 14 do not introduce new matter. Applicants specifically direct the Examiner's attention to Table 14 and 15, wherein the conditions at pH 5.0 are explicitly supported by the specification.

Accordingly, the rejection of the amendment filed January 11, 2002, under 35 U.S.C. §132, is overcome and withdrawal thereof is respectfully requested.

Claim 6 has been rejected under 35 U.S.C. §112, second paragraph, as allegedly unclear. The Examiner alleges that it is unclear which chemical structures are encompassed by "derivatives or homologs" of LIF. Specifically, the Examiner alleges that Page 4 of the specification, which teaches derivatives and homologs of LIF, was missing in the previous response.

In response, applicants have provided a duplicate copy of Page 4 in the response and specifically direct the Examiner's attention to the specification at Page 4, Line 19 to Page 5, Line 7 which provides a specific description of derivatives and homologs of LIF. It is believed that page 4 was timely provided to the U.S. Patent and Trademark Office at the filing date of the application (see attached postcard), but may have been inadvertently become detached or separated during processing at the U.S. Patent and Trademark Office.

Accordingly, the rejection of Claim 6 under 35 U.S.C. §112, second paragraph, is overcome and withdrawal thereof is respectfully requested.

Claims 1-3, 6-13, 15, 16, 20-26, 28, 29, 32, 34-40 and newly added claims 47, 50, 51 have been rejected as allegedly anticipated by Patterson et al.. Specifically, the Examiner alleges that the Declaration of Dr. Susan Ann Charman pursuant to 37 CFR 1.131 was inappropriate because MPEP §715 teaches that a prior invention may not be established under 1.131 if the rejection is based upon a U.S. patent to another which claims the same patentable invention as

the instant claims.

In response, applicants respectfully submit that, while the recitation of MPEP §715 was correctly cited, the Examiner's interpretation of the rule is not correct. The rejected claims were not claimed, but only shown or described, by Patterson et al. Applicants believe that the Declaration was both properly submitted and legally sufficient in the present circumstances.

Accordingly, the rejection of Claims 1-3, 6-13, 15, 16, 20-26, 28, 29, 32, 34-40 and newly added claims 47, 50-51 under 35 U.S.C. §102(e) is overcome and withdrawal thereof is respectfully requested.

Claims 1-3, 6-18, 20-26, 28-30, 32, 34-55 and newly added claims 44-55 have been rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Patterson et al. in view of Cleland.

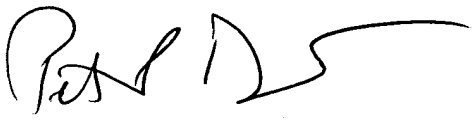
In response, applicants believe that this rejection is overcome based on the removal of Patterson et al. as a reference.

Accordingly, the rejection of Claims 1-3, 6-18, 20-26, 28-30, 32, 34-55 and newly added claims 44-55 under 35 U.S.C. §103(a) is overcome and withdrawal thereof is respectfully requested.

Attached is a marked-up version of the changes made to the specification which is captioned "VERSION WITH MARKINGS TO SHOW CHANGES MADE".

Thus, in view of the foregoing amendments and remarks, applicants respectfully submit that the present application is in condition for allowance, which action is earnestly solicited.

Respectfully submitted,



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Enclosures Version with Markings
Postcard
Page 4 of Specification (in duplicate)

"VERSION WITH MARKINGS TO SHOW CHANGES MADE"

IN THE SPECIFICATION:

The paragraph beginning at page 2, line 19 and ending at page 2, line 23 has been replaced as follows:

One aspect of the present invention contemplates a composition comprising leukaemia inhibitory factor (LIF) or a derivative or homologue thereof and a stabilizing agent facilitating chemical and/or physical stability of LIF in the composition, [additives for maintaining pH and isotonicity] and one or more pharmaceutically acceptable carries and/or diluents.

The paragraphs beginning at Page 5, Line 10 and ending at Page 5, Line 25 have been deleted.

The paragraph beginning at page 10, line 21 and ending at page 10, line 25 has been replaced as follows:

The compositions of the present invention achieve their stability through judicious choice of pH conditions within the range of from about 3.5 to about 6.5 inclusive and optionally the presence of one or more suitable stabilizing agents [and/or additives]. Preferably, the pH range is between from about 4.0 - 6.0 inclusive, more preferably between from about 4.5 to about 5.5 inclusive. Most preferably, the pH of the composition is about 5.0.

The paragraph beginning at page 11, line 33 and ending at page 12, line 7 has been replaced as follows:

The carrier [and other ingredients of the composition] must be pharmaceutically "acceptable" in the sense of being compatible with the other ingredients of the composition and not injurious to the subject. The compositions may conventionally be presented in unit dosage form and may be prepared by any methods well known in the art of pharmacy. Such methods include the step of bringing into association the active ingredient with the carrier which constitutes one or more accessory ingredients. In general, the compositions are prepared by uniformly and intimately bringing into association the active ingredient with liquid carriers of finely divided solid carriers

or both, and then if necessary shaping the product.

The paragraph beginning at page 12, line 27 and ending at page 12, line 33 has been replaced as follows:

Compositions suitable for parenteral administration include aqueous and non-aqueous isotonic sterile injection solutions which may contain anti-oxidant, buffers, [preservatives] bactericides and solutes which render the composition isotonic with the blood of the intended recipient; and aqueous and non-aqueous sterile suspensions which may include suspending agents and thickening agents. The compositions may be presented in unit-dose or multi-dose sealed containers, for example, ampoules and vials, and may be stored in a freeze-dried (lyophilised) condition to detect changes in chemical and physical degradation.

The paragraph beginning at page 14, line 11 and ending at page 14, line 15 has been replaced as follows:

The inventors examined a number of pH levels and [additives] stabilizing agents. Samples at pH 4.0, 4.5, 5.0, 5.5 and 6.0 were prepared in Examples 1 and 2, as described hereinafter, and additional [additives] stabilizing agents, Sorbitol, an isotonicity agent, and Polysorbate 80 (also referred to as Tween-80), as a non-ionic surfactant to reduce non-specific adsorption into surfaces, including glass, were also included. NaCl was also examined as an isotonicity agent.

The paragraph of "I. Sample Preparation" on page 49 has been replaced as follows:

I. Sample Preparation

8°C and 25°C LIF Samples

LIF formulations were prepared by a dilution of stock LIF (3.67 mg/ml in 2 mM phosphate buffer) with citrate buffer containing sorbitol or NaCl to give a final LIF concentration of 0.05 or 0.4 mg/ml, a final buffer concentration of 10 mM, a final sorbitol concentration of 5% w/v or a final NaCl concentration of 0.9% w/v. The theoretical pH was 5.0 in all cases. Formulations were prepared and filled into vials as described previously.

The first paragraph of "III. Results" has been replaced as follows:

III. Results

Ion Exchange

IEC data for 0.4 mg/ml formulations are shown in Tables 20 and 21. The results expressed as a percentage of the initial concentration remaining after the storage period indicated that the most stable formulations were the pH 5.0 citrate buffer containing sorbitol and Tween 80 and the pH 5.0 citrate buffer containing NaCl. The least stable was the pH 5 citrate buffer containing only sorbitol and pH 5.5 citrate containing sorbitol and Tween 80 was somewhere in the middle.

PATENT OFFICE DATE STAMP ACKNOWLEDGES RECEIPT OF:

1. Courtesy Copy of International Application
2. 5 (five) Formal Drawings
3. Transmittal W/Certificate of Express Mailing in Dupl.
4. Copy of International Search Report
5. Copy of International Preliminary Examination Report
6. Check in the Amount of $1,592.00
7. Express Mailing Label No.: EL308568422US
8. Preliminary Amendment

09/555108

Applicant: Susan Ann Charman, et al.
For: COMPOSITIONS OF LEUKAEMIA INHIBITORY FACTOR
Filed: Herewith
Docket: 13627
Dated: May 24, 2000
EWG:LP:am Serial No.: _ _____